**Supporting Information**

**Experimental and theoretical investigation of GS-441524 using Density Functional Theory, FTIR, Raman, and UV-VIS spectroscopy**

|  |  |  |
| --- | --- | --- |
| **Tables** | **Title**  | **Page** |
| S1 | B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å. | 2 |
| S2 | BP86/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å. | 3 |
| S3 | CAM-B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å. | 4 |
| S4 | Vibrational assignment for the experimentally observed FT-IR and Raman wavenumbers (cm-1) and comparison with BP86/6-311++G(d,p) calculations. Relative intensities are denoted by vs (very strong), s (strong), m (medium), m-s (medium to strong), w (weak), vw (very weak), and vr (variable), N/A (not available in the literature). The width of the peak is denoted by b (broad), and sh (sharp). In the case where an assignment can be allocated for two peaks, the second time is written as revised (rev.). Unless noted otherwise, the third column (vibration type) refers to intensities in infrared from the literature [Socrates, 2001], and the fourth column refers to vibration types obtained using the GaussView animations from the theoretical calculations from this work. | 5 |
| S5 | Atomic charge analysis of GS-441524 in water at B3LYP/6-311++G(d,p)level of theory. | 12 |

|  |  |  |
| --- | --- | --- |
| **Figures** | **Title**  | **Page** |
| S1 | Surface plot of the electrostatic potential of GS-441524 in water solvent at the B3LYP/6-311++G(d,p) level of theory. | 14 |

**Table S1.** B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -3.99344300 | -0.29053800 | 0.54425900 |
| O2 | -1.94438400 | -1.13429000 | 2.04713100 |
| H3 | -1.15577800 | -1.43134100 | 2.51127100 |
| O4 | -1.32467800 | 0.26160700 | -1.21792000 |
| O5 | -1.22164200 | 2.93341800 | -0.03873800 |
| H6 | -0.42728800 | 2.37723900 | -0.12551700 |
| N7 | 5.04280700 | -0.22448000 | 0.11382000 |
| H8 | 5.78756000 | 0.45295700 | 0.16409300 |
| H9 | 5.25857400 | -1.16263900 | -0.17584700 |
| N10 | 1.40667300 | -0.06368100 | -0.04209800 |
| N11 | 3.57686500 | 1.53375800 | 0.32247400 |
| N12 | 1.19668700 | 1.26986600 | 0.16691200 |
| N13 | -2.21423700 | -3.01025600 | -0.94542700 |
| C14 | 2.50672700 | -2.01244100 | -0.29921700 |
| H15 | 3.28583900 | -2.75432600 | -0.37640000 |
| C16 | -1.60499500 | -0.17349700 | 1.07154200 |
| H17 | -0.88426600 | 0.55289700 | 1.45108000 |
| C18 | 2.67594600 | -0.65063400 | -0.07410500 |
| C19 | 3.77226000 | 0.23881300 | 0.11708600 |
| C20 | 1.12687500 | -2.23906500 | -0.41025300 |
| H21 | 0.64267000 | -3.18374800 | -0.59957100 |
| C22 | -2.18366700 | 2.48939500 | -0.97878400 |
| H23 | -1.85012400 | 2.66657500 | -2.00981800 |
| H24 | -3.09040100 | 3.07781200 | -0.81295800 |
| C25 | -2.86645200 | 0.56842200 | 0.60418600 |
| H26 | -3.06381500 | 1.42729000 | 1.25307600 |
| C27 | -1.02823400 | -0.75299700 | -0.26887100 |
| C28 | -1.71760000 | -2.02016800 | -0.62834800 |
| C29 | 0.45426600 | -1.02822400 | -0.24839200 |
| C30 | -2.51493400 | 1.01267900 | -0.82453400 |
| H31 | -3.33539400 | 0.73390600 | -1.49225100 |
| C32 | 2.29626000 | 1.96188000 | 0.33676000 |
| H33 | 2.14089300 | 3.02187500 | 0.50527500 |
| H34 | -3.99557000 | -0.84150700 | 1.33751400 |

**Table S2.** BP86/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -4.00228600 | -0.29839700 | 0.51768700 |
| O2 | -1.96161700 | -1.10291000 | 2.06425400 |
| H3 | -1.15241500 | -1.46517000 | 2.46284200 |
| O4 | -1.33267300 | 0.26361100 | -1.24200800 |
| O5 | -1.18309100 | 2.92650200 | -0.00270000 |
| H6 | -0.39624400 | 2.33607500 | -0.09754000 |
| N7 | 5.05943600 | -0.24364000 | 0.12549200 |
| H8 | 5.80402400 | 0.44838700 | 0.14610000 |
| H9 | 5.27665800 | -1.18064200 | -0.19499900 |
| N10 | 1.40371300 | -0.06732700 | -0.04534900 |
| N11 | 3.59551900 | 1.53475000 | 0.31066000 |
| N12 | 1.19532300 | 1.27350800 | 0.15112200 |
| N13 | -2.23893700 | -3.02617600 | -0.92900200 |
| C14 | 2.49988700 | -2.03813900 | -0.28654900 |
| H15 | 3.28018300 | -2.79228500 | -0.35451700 |
| C16 | -1.61381100 | -0.15011300 | 1.07082300 |
| H17 | -0.88374700 | 0.58832500 | 1.44072900 |
| C18 | 2.68066900 | -0.66667900 | -0.06953800 |
| C19 | 3.78173600 | 0.22307500 | 0.11517100 |
| C20 | 1.11323600 | -2.25749100 | -0.40133500 |
| H21 | 0.61614100 | -3.20652800 | -0.58739400 |
| C22 | -2.15058000 | 2.51463500 | -0.96335900 |
| H23 | -1.80419100 | 2.69895800 | -1.99987200 |
| H24 | -3.05360600 | 3.12581400 | -0.79650400 |
| C25 | -2.88150300 | 0.58279700 | 0.59363300 |
| H26 | -3.09463900 | 1.44589600 | 1.24998600 |
| C27 | -1.04158000 | -0.74988200 | -0.27223200 |
| C28 | -1.73798100 | -2.02166800 | -0.61287700 |
| C29 | 0.44106300 | -1.03421000 | -0.24879200 |
| C30 | -2.51867100 | 1.03888500 | -0.83208700 |
| H31 | -3.35003900 | 0.78170200 | -1.51144500 |
| C32 | 2.31150200 | 1.96710300 | 0.31907400 |
| H33 | 2.15423000 | 3.03751800 | 0.47843800 |
| H34 | -3.96819400 | -0.87619600 | 1.30425600 |

**Table S3.** CAM-B3LYP/6-311++G(d,p) optimized geometry of GS-441524. The X, Y, and Z coordinates are in Å.

|  |  |  |  |
| --- | --- | --- | --- |
| **Atom** | **Χ** | **Υ** | **Ζ** |
| O1 | -3.96228000 | -0.30067400 |  0.52548100 |
| O2 | -1.93575700 | -1.12350700 |  2.02792500 |
| H3 | -1.15022200 | -1.44697900 |  2.47612300 |
| O4 | -1.31574700 | 0.27210300 |  -1.20992600 |
| O5 | -1.19989100 | 2.89899800 |  -0.00636100 |
| H6 | -0.40758100 | 2.34357900 |  -0.10402900 |
| N7 | 5.01414500 | -0.23439000 |  0.10534100 |
| H8 | 5.76686500 | 0.42793900 |  0.19871500 |
| H9 | 5.22143600 | -1.19346200 |  -0.10827800 |
| N10 | 1.39816000 | -0.06597500 |  -0.04611100 |
| N11 | 3.56108700 | 1.52204400 |  0.30976500 |
| N12 | 1.19261100 | 1.26529300 |  0.15292400 |
| N13 | -2.21145500 | -2.99031600 |  -0.93407800 |
| C14 | 2.48703100 | -2.00797200 |  -0.28855500 |
| H15 | 3.26489100 | -2.75071900 |  -0.36344000 |
| C16 | -1.59703100 | -0.16333800 |  1.06194300 |
| H17 | -0.87888700 | 0.56390200 |  1.44281800 |
| C18 | 2.65489100 | -0.65224800 |  -0.07290900 |
| C19 | 3.75396700 | 0.23516100 |  0.11488200 |
| C20 | 1.10937200 | -2.23187000 |  -0.39897000 |
| H21 | 0.62192100 | -3.17535200 |  -0.58426900 |
| C22 | -2.15786900 | 2.48916100 |  -0.95492200 |
| H23 | -1.81629800 | 2.67911800 |  -1.97944000 |
| H24 | -3.05892900 | 3.08259400 |  -0.78404400 |
| C25 | -2.85453400 | 0.56965700 |  0.59556900 |
| H26 | -3.06533000 | 1.42314200 |  1.24521000 |
| C27 | -1.02829500 | -0.73784400 |  -0.26931400 |
| C28 | -1.72190500 | -2.00096400 |  -0.62653600 |
| C29 | 0.44720000 | -1.02362800 |  -0.24634100 |
| C30 | -2.49771900 | 1.01962300 |  -0.82278100 |
| H31 | -3.31643900 | 0.75006100 |  -1.49443900 |
| C32 | 2.28307500 | 1.95390800 |  0.31788000 |
| H33 | 2.13096500 | 3.01501900 |  0.47860400 |
| H34 | -3.95392100 | -0.86868200 |  1.30495100 |

**Table S4.** Vibrational assignment for the experimentally observed FT-IR and Raman wavenumbers (cm-1) and comparison with BP86/6-311++G(d,p) calculations. Relative intensities are denoted by vs (very strong), s (strong), m (medium), m-s (medium to strong), w (weak), vw (very weak), and vr (variable), N/A (not available in the literature). The width of the peak is denoted by b (broad), and sh (sharp). In the case where an assignment can be allocated for two peaks, the second time is written as revised (rev.). Unless noted otherwise, the third column (vibration type) refers to intensities in infrared from the literature [Socrates, 2001], and the fourth column refers to vibration types obtained using the GaussView animations from the theoretical calculations from this work.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Experimental $\tilde{ν}$ IR | Experimental $\tilde{ν}$ Raman | Vibration type | Theoretical $\tilde{ν}$ IR | Theoretical $\tilde{ν}$ Raman |
| 3471 s, sh  | - | 3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols) | 3718 vw stretching C(2')O-H | 3718 m, sh |
| 3425 s, sh | - | 3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols)3670 - 3580 vr+m-s, b or sh Ο-Η stretching (alcohols) | 3651 vw stretching C(3')O-H | 3651 m, sh |
| 3334 s, sh  | - | 3520 - 3420 m, b Ν-Η asymmetric stretching (primary aromatic amine)  | 3636 vw Ν-Η asym. stretching | 3636 m, sh |
| 3228 m | - | 3420 - 3340 m, b Ν-Η symmetric stretching (primary aromatic amine)  | 3505 w, sh Ν-Η sym. stretching | 3505 m, sh |
| 3186 m, br | - | 3670 - 3580 vr+m-s, b or shΟ-Η stretching (alcohols) | 3404 vs, sh stretching C(5')O-H We note that C(5')O-H makes an H-bond with N-1 of triazine as their H distance from O/N is smaller than 3.5 Å reducing the observed frequency. | 3404 vs, sh |
| 3084 | 3056  | 3100 -3010 m =C-H stretching (pyrrole) 3100 - 3000 m C-H stretching of triazine  | 3179 vwsym. stretching Η-C-C-H of pyrrole ring3163 vwasym. stretching Η-C-C-H of pyrrole ring3108C-H stretching of triazine | 3179 m, sh3163 (m, sh) 3108 m, sh |
| 2948 w | 2937 vw | 2990 - 2900 vr+m-w C-H asym. stretching (CH2 in primary alcohols (CH2-ΟΗ))  2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2993 vw asym stretching C-H in primary alcohols & C-H stretching of tetrahydrofuran2990 vwC-H stretching of tetrahydrofuran | 2993 s, sh2990 m, sh |
| 2908 w | 2913 vw  | 2990 - 2900 vr+w-m C-H asym. stretching (CH2 in primary alcohols (CH2-ΟΗ))  2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2972 vw asym. stretching C-H of primary alcohol & C-H stretching of tetrahydrofuran2950 vwC-H stretching of tetrahydrofuran | 2972 s, sh2950 s, sh |
| 2852w | - | 2935 - 2840 vr+w-m C-H sym. stretching of primary alcohols (CH2-ΟΗ) 2980 - 2700 m-s Tetrahydrofurans, multiple peaks | 2913 vwsym stretching C-H of primary alcohol & C-H stretching of tetrahydrofuran | 2913 s, sh |
| 2763 w2717 w | - | 2980 - 2700 m-s Tetrahydrofurans, multiple peaks | - | - |
| 2243 vw  | 2245 w | 2260 - 2200 vr+ (from vw to vs), sh -C$≡$N stretching | 2245 vw-C$≡$N stretching | 2245 s, sh |
| 1658 vs1610 s | 1664 vw1605 vw | 1615-1580 (Ν/Α) Ν-Η deformation of ΝΗ2 (in aromatic amines) 1608 m-s C=N stretching of triazine ring[Alrooqi, 2022]1558 in-plane and totally symmetric stretching of N3C2 and C5C6 in the triazine ring, [Thastum Bach99] | 1599 s, sh Ν-Η deformation (scissoring) of aromatic ΝΗ2in-plane stretching of triazine ring or heterocyclic base | 1599 vw  |
| 1539 s shoulder at 1518  | 1541 w1519 w1479 vs shoulder at 1453  | 1625-1430 vr+m-s C=C stretching of aromatic rings  | 1489 w, bstretching of aromatic heterocyclic rings | 1489 s, sh |
| 1475 s, sh shoulder at 1450 1379 w1358 w 1334 s | 1479 vs shoulder at 1453 (rev.)1422 m1364 w, sh1350 s, sh | 1625-1430 vr+m-s C=C stretching of aromatic rings1450 – 1350 vr out-of-plane deformation of triazine ring 1360-1250s-m C(aromatic)-N stretching in primary aromatic amine  | 1452 w, basym stretching of triazine ring-C-C(Ν)- stretching of aromatic heterocyclic ring | 1452 s, sh |
| 1298 w-m, sh1277 w, sh1261 w, sh1228 w1167 w, sh1136 m, sh1107 w, sh1088 m, sh shoulder at 1074  | 1299 m, sh1273 w-m shoulder at 1263 1169 m1135 vw1107 w | 1290-990 s in-plane deformation of aromatic rings 1100 -1075 s C-O stretching (tetrahydrofurans)  | 1071 w, bin-plane ring deformationC-O stretching of pyrrole | 1071 w, b |
| 1049 w, sh1016 vs, br | 1016 w, sh shoulder at 1009  | 1290-990 s in-plane deformation of aromatic rings1100 -1075 s C-O stretching (tetrahydrofurans) 1000-980 w Stretching of triazine ring  | 1034 w, bΗ-C-C-H scissoring of pyrroleC-O stretching (tetrahydrofurans)Η-N-H rocking of amine | 1034 w, b |
| 1016 vs, br (rev.)906 m, sh | 1016 m shoulder at 1009 (rev.)906 w-m | 1290-990 s in-plane deformation of aromatic rings 1090-1000 s C-O stretching (primary alcohols)1000-980 w stretching of triazine ring | 981 w, bΗ-C-C-H scissoring of pyrrolestretching of triazine ringΗ-Ν-Η rocking of amineC-O stretching (tetrahydrofurans) | 981 w, b |
| 906 m, sh (rev.)860 m-s, sh787 m-s, sh shoulder at 775729 s704 w shoulder at 678 607 w577 w540 w | 906 w-m (rev.)780 w-m 717 s705 s639 w-m620 w-m581 w544 w | 900-650 s stretching of aromatic rings 595 s deformation of furan ring | 694 vwbreathing of the whole molecule | 694 w, b |
| - | 433 w396 w-m358 w-m328 w-m252 w 211 w-m | 445-345 vr+w-m in-plane stretching of the bond aromatic ring – NH2 (in primary amines)390-330 m C-O put of plane deformation in secondary alcohols  | 259 s, sh | 259 vw |
| - | 153 w-m | - | 168 s, sh-ΟΗ deformation (secondary alcohols) and of furan ring | 168 vw |

**Table S5.** Atomic charge analysis of GS-441524 in water at B3LYP/6-311++G(d,p) level of theory.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Atom | Mulliken | CHelp | CHelpG | HLYGAt | MK |
| O1 | -0.226534 | -0.722152 | -0.775213 | -0.692774 | -0.710689 |
| O2 | -0.274071 | -0.669168 | -0.762110 | -0.705694 | -0.739593 |
| H3 | 0.312760 | 0.418991 | 0.465279 | 0.496170 | 0.487417 |
| O4 | -0.058908 | -0.610792 | -0.557800 | -0.359660 | -0.403893 |
| O5 | -0.381642 | -0.732038 | -0.716342 | -0.681570 | -0.700163 |
| H6 | 0.433436 | 0.326195 | 0.393466 | 0.416124 | 0.394827 |
| N7 | -0.392493 | -1.036757 | -1.047790 | -1.095260 | -1.090738 |
| H8 | 0.354506 | 0.417009 | 0.466467 | 0.479753 | 0.479980 |
| H9 | 0.318726 | 0.485569 | 0.474619 | 0.498538 | 0.493397 |
| N10 | 0.584084 | 0.591527 | 0.593161 | 1.032314 | 0.890515 |
| N11 | -0.239521 | -0.766739 | -0.859322 | -0.929738 | -0.903517 |
| N12 | -0.401223 | -0.516407 | -0.664993 | -0.810230 | -0.736113 |
| N13 | -0.282268 | -0.551425 | -0.557199 | -0.599054 | -0.594937 |
| C14 | -0.284529 | -0.131905 | -0.125168 | -0.110926 | -0.121292 |
| H15 | 0.214370 | 0.133539 | 0.142382 | 0.183987 | 0.175945 |
| C16 | -0.735631 | 0.121817 | 0.225621 | 0.145392 | 0.285203 |
| H17 | 0.275624 | 0.011439 | 0.015354 | 0.104627 | 0.045647 |
| C18 | 0.399941 | -0.413654 | -0.357929 | -0.708033 | -0.596944 |
| C19 | -0.211908 | 1.011575 | 0.991633 | 1.168021 | 1.121029 |
| C20 | -0.129412 | -0.090703 | -0.166922 | -0.235139 | -0.219469 |
| H21 | 0.202351 | 0.116247 | 0.145480 | 0.193271 | 0.188944 |
| C22 | -0.703041 | 0.645899 | 0.277703 | 0.094759 | 0.221478 |
| H23 | 0.186895 | -0.089358 | 0.008416 | 0.070911 | 0.024302 |
| H24 | 0.185752 | -0.117859 | 0.022381 | 0.102482 | 0.056714 |
| C25 | -0.565745 | 0.542448 | 0.449571 | 0.195118 | 0.221577 |
| H26 | 0.269021 | -0.079378 | -0.026618 | 0.102866 | 0.062753 |
| C27 | 0.829064 | 0.723880 | 0.463528 | -0.104253 | -0.017422 |
| C28 | -0.802811 | 0.371307 | 0.433173 | 0.686847 | 0.625542 |
| C29 | -0.310310 | -0.425515 | -0.275137 | -0.258788 | -0.257079 |
| C30 | 0.601499 | 0.083245 | 0.156278 | 0.034275 | 0.110746 |
| H31 | 0.287308 | 0.021997 | 0.047180 | 0.131497 | 0.090992 |
| C32 | 0.034425 | 0.513406 | 0.610194 | 0.601948 | 0.559808 |
| H33 | 0.234083 | 0.017701 | 0.042747 | 0.083724 | 0.089126 |
| H34 | 0.276202 | 0.400059 | 0.467909 | 0.468496 | 0.465909 |

****

**Fig. S1.** Surface plot of the electrostatic potential of GS-441524 in water solvent at the B3LYP/6-311++G(d,p) level of theory.